UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/727,770	12/04/2000	Znenya Li	CL000651	5477

25748 7590 11/20/2003

CELERA GENOMICS CORP.
ATTN: WAYNE MONTGOMERY, VICE PRES, INTEL PROPERTY
45 WEST GUDE DRIVE
C2-4#20
ROCKVILLE, MD 20850

EXAMINER	
SULLIVAN, DANIEL M	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 11/20/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/727,770	LI ET AL.	
	Examiner	Art Unit	
	Daniel M Sullivan	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 August 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4,8,9 and 24-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) ~~4~~ *8,9 and 24-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 August 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

This Non-Final Office Action is a response to the "Response to 1st Office Action" filed 15 August 2003 (hereinafter, 15 August Paper) in reply to the Non-Final Office Action mailed 24 February 2003 (hereinafter, 24 February Office Action). Claims 4, 8, 9 and 24-29 were considered in the 24 February Office Action. Claims 4, 8, 9 and 24-29 are pending and under consideration herein.

Response to Amendment

Objection to the specification as containing informalities is withdrawn.

Response to Arguments and New Grounds for Rejection.

Claim Rejections - 35 USC § 101

The previous Office Action indicates that the claims have been rejected under 35 U.S.C. §101 and §112, first paragraph, because the claimed invention is not supported by a credible asserted utility or a well-established utility. Although the body of the rejection sets forth grounds for rejection as lacking specific and substantial credible utility, the omission of specific and substantial from the introductory paragraph might have given the impression that the rejection was based on incredible utility. Therefore, the rejection under 35 U.S.C. §101 is again set forth with expanded arguments to clearly indicate that the claims are rejected because the claimed invention lacks a specific and substantial credible utility, and to address the arguments in Applicant's response. This Office Action is made non-final to allow Applicant an opportunity to fully respond to the argument set forth herein below.

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 4, 8, 9 and 24-29 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial credible asserted utility or a well-established utility.

The claims are directed to an isolated nucleic acid molecule consisting of the sequence set forth as SEQ ID NO: 1 and 3, and a nucleic acid molecule encoding a polypeptide comprising the amino acid sequence set forth as SEQ ID NO: 2.

Several teachings were cited in the previous Office Action which demonstrate the unpredictability of assigning protein function based on structure alone (see especially the discussion bridging pages 5-6). Given this unpredictability and the low degree of sequence homology of the instant SEQ ID NO: 2 to ATP synthase 16 kDa proteolipid subunits relative to the homology found among ATP synthase 16 kDa proteolipid subunits, the skilled artisan would not predict that the instant SEQ ID NO: 2 would, more likely than not, have the function of an ATP synthase 16 kDa proteolipid subunit. In the absence of an established function for the claimed nucleic acid, the claimed invention lacks a readily apparent utility because the skilled artisan would not know what the protein does.

Applicant contends that the figure sheets provide support to the functional claim of the present invention. Applicant points to Prosite data which allegedly provide the functional domain of the protein of the present invention such as the protein kinase C phosphorylation site and

casein kinase II phosphorylation site. Applicant further argues that the Hummer search result shows that the protein of the present invention has statistically significant domain of ATP synthase subunit C, and the cites Exhibit 1, filed with the present Amendment, as revealing that the present invention has 52% homology with tomato vacuolar proton translocating ATPase (see Exhibition 1). Applicant urges that these showings indicate that the domain of the ATPase of the present invention is highly conserved.

These arguments have been fully considered but are not found persuasive because the evidence of record, viewed as a whole, does not support Applicant's contention that the claimed invention encodes a vacuolar ATP synthase subunit. As pointed out in the previous Office Action, polypeptide having the function of a vacuolar ATP synthase subunit have a high degree of structural conservation, and even an insect vacuolar ATP synthase subunit C is more closely related to the human vacuolar ATP synthase than is the polypeptide encoded by the instant claimed nucleic acid, which is also of human origin. Applicant alleges that, in spite of this, the asserted function is reasonable because the polypeptide encoded by the claimed nucleic acid comprises conserved functional domains. However, the functional domains identified by Applicant (i.e., a protein kinase C and casein kinase II phosphorylation sites, and an ATPase domain) are found in proteins having widely divergent functions. Protein kinase C and casein kinase II are known to phosphorylate many different proteins and the examiner is unaware of any established nexus between phosphorylation by protein kinase C or casein kinase II and function as a vacuolar ATP synthase subunit C. Likewise, many proteins are known to comprise ATPase domains (see, e.g., enzymes found within EC numbers 3.6.1 and 3.6.4), the vast majority of which do not have the function of a vacuolar ATP synthase. Thus, the functional domains

comprised by the protein encoded by the claimed nucleic acid are generic to proteins having widely divergent function and do not support the asserted function as a vacuolar ATP synthase subunit.

Applicant asserts that the claimed isolated nucleic acid molecules and methods of making and using such nucleic acid molecules have several uses that meet the requirements of 35 U.S.C. § 101 and the first paragraph of 35 U.S.C. § 112 because these methods of making and using, and the accepted state of the art view that such molecules have uses within the commercial marketplace in the drug development cycle because they encode previously unidentified members of important pharmaceutical targets, establishes the utility of the claimed invention.

This argument is not persuasive because the utilities asserted in the specification are neither specific nor substantial. Beginning on page 44, the specification teaches a variety of uses for the claimed nucleic acid molecules, including: probing for related nucleic acids; probing to determine chromosomal position; probing to determine expression levels; PCR amplification of portions of the nucleic acid molecule; constructing recombinant vectors including expression vectors; expression of the encoded protein or antigenic portions thereof for the purpose of protein purification, drug screening or to raise antibodies; diagnostic assays; and treatment. However, the disclosure fails to teach the skilled artisan, specifically, what real world problem will be addressed. In particular, although the specification devotes the majority of the discussion of utility to diagnosis and treatment of disease, there is not a single example of a disease that can be treated using the claimed invention or molecules that interact with the polypeptide encoded thereby. Instead the specification teaches that these molecules will be used to diagnose or treat "transporter-related conditions that are specific for the subfamily of transporters that are one of

the present invention belongs to, particularly in cells and tissues that express the transporter" (paragraph bridging pages 27-28). This is far from a teaching of specific and substantial utility. Instead, it is an invitation to the skilled artisan to discover for himself "transporter-related conditions that are specific for the subfamily of transporters that are one of the present invention belongs to", and then devise a diagnostic or therapeutic approach to that condition. "Utilities that require or constitute carrying out further research to identify or reasonably confirm a 'real world' utility are not substantial utilities" (see M.P.E.P. 2107.01 (I)).

As pointed out in the previous Office Action, "probing for related nucleic acid molecules or expression levels is not useful unless some functional meaning can be attributed to the relatedness or expression of the identified nucleic acid molecules; expressing a protein that has no known function has no specific utility other than to determine what that protein does; results from a diagnostic assay are not useful if the findings cannot be correlated with a pathological state; and a method of treatment is not useful without knowing what patient population can be treated according to the method" (paragraph bridging pages 4-5).

In the 15 August Paper, Applicant cites *Nelson v. Bowler*, 206 USPQ 881 (CCPA 1980) and contends that a showing of less than a specific therapeutic use of a claimed chemical compound satisfies the utility requirement. However, the facts in *Nelson v. Bowler* are clearly different from the facts in the instant case. In *Nelson v. Bowler*, the CCPA found that the pharmacological activity demonstrated by Nelson was sufficient to satisfy the utility requirement of 35 U.S.C. §101 because, "knowledge of the pharmacological activity of any compound is obviously beneficial to the public". However, in the instant case, no pharmacological activity has been demonstrated. Applicant merely speculates that, because the claimed nucleic acid encodes a

naturally occurring protein and proteins are frequently targets of therapeutic agents, the polypeptide encoded by the claimed nucleic acid must also be a target of therapeutic agents.

Furthermore, conditions that might be amenable to treatment with the compounds of Nelson would be readily apparent to the skilled artisan from the pharmacological activity described in the application (i.e., pressor effect *in vivo*). That is not the case here, as clearly indicated by the absence of even speculative discussion of what conditions might be amenable to treatment or diagnosis using the claimed invention or agents obtained therewith. Applicant argues, "[i]t is well recognized that transporters are the most important targets for drug action" (page 4). Even if this were true, however, the therapeutic application of any pharmaceutical that acts at a transporter is highly dependent on the particulars of the transporter. For example, the effect of administering an inhibitor of the sodium-potassium ATPase, such as a cardiac glycoside used in the treatment of heart failure, are dramatically different from effects of administering a proton pump inhibitor, such as those used to treat stomach ulcers and esophagitis. Thus, simply knowing that a nucleic acid encodes some form of transporter does not provide the skilled artisan with a specific and substantial utility. Furthermore, even if the asserted function of the polypeptide encoded by the claimed invention were true (i.e., it is a component of a vacuolar ATP synthase), the examiner can find nothing in the art that would direct the skilled artisan to treatment or diagnosis of a specific condition.

Next, Applicant cites *Juicy Whip v. Orange Bang*, 51 USPQ2d 1700 (CAFC 1999) and contends, "*Juicy Whip* held that, in order to violate the utility requirement, an invention must be 'totally incapable of achieving a useful result'" (page 5). This argument is not found persuasive because, in order to meet the utility requirement of 35 U.S.C. §101, the disclosure must provide a

specific and substantial credible utility. The statement in *Juicy Whip* is actually a quote from *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 24 USPQ2d 1401 (Fed. Cir. 1992) wherein the question at hand was whether the invention was operable (i.e., whether the asserted utility was credible). In the instant case, the issue at hand is not whether the asserted utility is credible but whether a specific or substantial utility has in fact been asserted. The Examiner's position is not that the claimed nucleic acid will never be useful, but that the disclosure fails to teach, in specific and substantial terms, what the claimed nucleic acid is to be used for.

Applicant argues, "novel transporter/nucleic acids are commercially useful for developing therapeutics/diagnostics for these and other pathologies...Not all nucleic acid molecules, and actually a very limited number, of the 3 billion bases that make up the human genome will encode a protein for these and the other disclosed uses. These uses are quite specific for the transporter family of proteins, even though each member may play a somewhat different role in cellular responses and pathologies. Even though each member may have a somewhat different role in biology and disease, each is a specific composition of matter having substantial, specific and credible uses that the vast majority of other isolated nucleic acid molecules do not possess" (page 5). This argument is not persuasive because, as pointed out previously, even if the claimed invention has utility, the skilled artisan does not know what that utility is and must go and discover it for himself. Applicant is reminded, "[l]aw requires that disclosure in application shall inform those skilled in the art how to use applicant's alleged discovery, not how to find out how to use for themselves" (*In re Gardner, Roe and Willey* 166 USPQ 138). Narrowing the universe of possible utilities to something less than infinite does not constitute a teaching of specific and substantial utility.

Applicant's arguments in the paragraph bridging pages 5-6 are philosophical in nature and do not speak to the particulars of the instant case. In the remaining paragraphs, Applicant sets forth examples of allegedly specific and substantial utilities that can be found in the specification. Applicant contends, "the present nucleic acid molecules can be used to produce protein targets for identifying agents that bind to the protein targets and modulate protein function. Such agents can be used to precisely determine which biological and pathological processes the protein is involved in. Furthermore, such agents that bind to a protein target and modulate cell signaling may subsequently be developed and refined for use in mammalian therapeutic applications." Thus, the asserted utility appears to be to identify agents that bind to the protein encoded by the invention, which can be used to determine what biological and pathological processes the protein is involved in and administered as a therapeutic. However, developing reagents that can be used to investigate the properties of the claimed invention or treat an unspecified disease is neither a specific nor substantial utility.

Applicant contends, "[i]n addition to serving as targets for developing molecular probes and therapeutic agents, the disclosed uses of the claimed nucleic acid molecules as probes, primers, and chemical intermediates, particularly in biological assays, is sufficient to satisfy the requirements of 35 USC §101 and §112" and "such uses are specific for the claimed nucleic acid molecules, and the products of such uses will be clearly different (and hence specific for the claimed molecules) than what would be produced using a different nucleic acid molecule for the same purpose." These arguments are not persuasive because the teachings of the specification are merely broad recitations of what could be done with any nucleic acid. Any nucleic acid molecule can be used as a probe, a primer, or a chemical intermediate. Although it is true that in the instant

case the probes, primers and final products would be unique to the instant nucleic acid, the utilities set forth in the specification are not based on the unique properties of the invention. For example, were the nucleic acid demonstrated to be linked to hypersecretion of stomach acid, the skilled artisan would know that the probes, primers and final products could be used to develop potential therapeutics for the treatment of esophagitis. That is not the case here. Instead, Applicant has disclosed a nucleic acid, the function of which is likely unknown, and teaches the skilled artisan that the nucleic acid is useful for the same things that any nucleic acid is useful for, because it is a nucleic acid. Applicant seems to be arguing that the specific utility of the invention is inherent to the nucleic acid and need not be described. This is akin to arguing that a teaching that a given transgenic mouse, comprising a specified gene, can be used as rat food constitutes a specific utility simply because the transgenic mouse is inherently different from other transgenic or wild type mice. Clearly this is not the case. A teaching of specific utility requires more than a general statement that a specific utility is likely to exist by virtue of the invention being different from other molecules belonging to the same class. Instead, the specific utility must actually be contemplated by the inventor.

Applicant's arguments are not found persuasive either individually or as a whole. Therefore, the claims stand rejected as lacking a disclosed specific and substantial credible utility.

Claims 4, 8, 9 and 24-29 are also stand rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial

credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

New Grounds

Claim Objections

Claim 9 is objected to because of the following informalities: The claim is directed to a genetically modified host cell. As the specification contemplates genetically modified host cells comprised within a transgenic animal (beginning on page 62), the claim encompasses a transgenic animal. As a transgenic animal is nonelected subject matter (see the restriction requirement mailed on 27 September 2002, the claimed host cell encompasses nonelected subject matter which should be removed from the claim. Amending the claim such that it is directed to "an isolated host cell" would be remedial. Appropriate correction is required.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel M Sullivan whose telephone number is 703-305-4448. The examiner can normally be reached on Monday through Friday 8-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 703-305-1998. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

DMS

Anne-Marie Falk

ANNE-MARIE FALK, PH.D.
PRIMARY EXAMINER